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A NEW BOOKLET

RICKETS DENTITION AND VITAMIN D

As early as the 17th century, Glissom associated rickets with delayed dentition, yet it has only been within recent years that investigators have been disposed to accept a common etiology for rickets and derangements in tooth structure and eruption.

This was doubtless due to the different modes of treatment prevailing between dentistry and medicine. However, extended research repeatedly produced clinical evidence that rickets and faulty dentition were concomitant.

Each came to be recognized as the end result of unbalanced metabolism—a nutritional deficiency—produced from lack of proper deposition of calcium and phosphorus in the skeletal structure of the child.

A forward step was thus achieved when the teeth were definitely regarded as part of the bony structure by both professions. It advanced sharply as the etiology and pathology became understood and knowledge was diffused.

In the light of modern research the relation of rickets to delayed dentition, malocclusion, hypoplasia, dental caries, and odontoclasia is too intimate to warrant a separation when a discussion of either subject is undertaken.

Investigations have by now clearly established the interdependence of physician and dentist in the prevention, treatment and cure of these conditions. A review of the literature in Rickets, Dentition, and Vitamin D has been made in this booklet to organize the findings of general research as related to their respective practices.

Send for this new booklet.

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THE SYNDROME PRODUCED BY ANEURYSM AT OR NEAR THE JUNCTION OF THE INTERNAL CAROTID ARTERY AND THE CIRCLE OF WILLIS[1]

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From the Medical Clinic of the Johns Hopkins Hospital and the Massachusetts General Hospital

In 1923 Symonds (1) published the case history of a woman[2] who died at the Peter Bent Brigham Hospital as a result of a ruptured aneurysm of the intracranial portion of the internal carotid artery. It was my privilege to see the case as a student, and what seemed most remarkable at the time was that Dr. Symonds made the diagnosis before death. Two cases have been seen since then, which, as a result of the teachings of Symonds (1, 2, 3), were easily recognized as instances of this same supposedly rare condition. A relatively short search of the literature reveals many more cases, some of which could be diagnosed in retrospect. It is the purpose of this paper to publish two new cases,[3] to give in abstract form the cases collected from the literature, and finally to focus attention on the clinical syndrome of this particular subgroup of intracranial aneurysms occurring at or near the junction of the internal carotid artery with the Circle of Willis.

The histories of the two new cases were as follows.

Case 1. J. H. H. No. 18756. A married white farmer of 33 was admitted to the Medical Service of the Johns Hopkins Hospital, June 1, 1928, complaining of pain behind his left eye of six weeks' duration.

The past history was essentially negative. He was born with a congenital deformity of the left hand (Fig. 1). He had had measles and mumps in childhood and gonorrhea in 1919. He had never had syphilis.

Six weeks before his admission the patient was suddenly seized, during coitus, with an excruciating pain localized in the region just above the left eye. The pain

[1] Received for publication October 18, 1928.

[2] See Case 25 for abstract.

[3] The first of these cases I saw while serving as an Assistant Resident Physician at the Johns Hopkins Hospital, and the second while serving as a House Officer at the Massachusetts General Hospital.

FIG. 1. CASE 1. CONGENITALLY DEFORMED LEFT HAND

UNIV. OF MICH.

was so severe that he rushed to the nearest doctor who gave him a hypodermic injection which only partially relieved the pain. Shortly after that he vomited. There was no loss of consciousness at any time. The pain was continuous throughout his illness, and spread slightly so that it involved the left side of the upper part

FIG. 2. CASE 1. PHOTOGRAPH OF PATIENT ON ADMISSION

of his nose. Three weeks before admission the patient awoke after an induced sleep to find that he could not open his left eye (Fig. 2). Examination of the eye showed that it was turned outward and that the pupil was dilated. This condition persisted.

Physical examination on admission showed a well developed, well nourished young man in severe pain. The pain was localized at the distribution of the ophthalmic branch of the left fifth cranial nerve. No objective sensory changes were elicited in this region. The left eyelid was completely ptosed and the left eye was rotated outward. The patient was unable to turn the eye inward. The fourth and sixth nerves were not affected. The left pupil was markedly dilated and failed to react to light or in accommodation. The fundi were negative. There was no stiff neck nor Kernig's sign. It was noted that the pain was relieved when the carotid artery on the left side was obliterated by pressure and that it returned immediately on release of pressure. The pain was not influenced by similar obliteration of the right carotid artery. The left hand was deformed, due to what appeared to be a congenital absence of the middle phalanges of the fingers (Fig. 1). The blood pressure was 120/78. The pulse varied in rate between 60 and 80. Neurological and general physical examinations were otherwise entirely negative.

The red blood cell count was 4,700,000, white blood cell count 5,600, and hemoglobin 82 per cent. The urine analysis showed nothing abnormal.

The impression on admission was recent rupture of an intracranial aneurysm, probably near the junction of the internal carotid artery with the Circle of Willis. The picture was incomplete in that the signs of meningeal irritation, stiff neck, Kernig's sign and others, resulting from subarachnoid hemorrhage, were absent. This, however, was disregarded because of the duration since onset.

Further study in the hospital added no positive information. The blood Wassermann was negative. X-rays of the skull were negative. Lumbar puncture revealed an initial pressure of 85 mm. of water with a prompt rise on compression of either jugular vein. The fluid was absolutely colorless when compared with water. There were no cells and no increase in globulin. The spinal fluid Wassermann was negative. Although there was considerable impairment of vision in the left eye due to inability to focus. the visual fields were found to be normal. The non-protein nitrogen in the whole blood was 31 mgm. per 100 cc.

Because of the marked relief obtained by pressure on the internal carotid artery, ligation on the left side was advised. Consequently on June 10 the patient was instructed to obliterate his left carotid artery with pressure until be became dizzy and to repeat this frequently. It was hoped in this way to establish a collateral circulation. On June 11, eleven days after admission, the patient complained of a generalized headache, especially in the occipital region, in addition to the previous pain. Examination showed a stiff neck and a positive Kernig's sign. This seemed to be almost certain evidence of a fresh subarachnoid hemorrhage and completed the diagnosis. Because of the possibility that this fresh leakage was induced by obliterating and releasing the carotid artery this procedure was discontinued. A second lumbar puncture was considered unsafe. The patient was transferred at once to the Neurosurgical Service.

The operation under local anesthesia was performed on June 12 by Dr. Walter Dandy. It was decided that only a partial occlusion of the carotid artery should

be attempted as the patient was just above the age at which ligation can be safely done. A small piece of fascia was removed from the thigh. The left internal carotid was exposed just above the bifurcation of the common carotid artery. It was surrounded by a double layer of fascia lata and this was sutured over the vessel thereby strangling it. There was still a pulse but no thrill. At no time during the operation did the patient experience any cerebral disturbances.

Several hours after the operation the patient became increasingly drowsy and later aphasic. A right hemiplegia developed and the respirations fell to 10. The ligature of fascia was loosened the evening of June 12 in a second operation. Following this the patient's general condition seemed to improve for about 36 hours and the respirations rose almost to normal. The aphasia and hemiplegia persisted, however. On June 15 the patient became very much worse. The ligature was completely removed in a third operation. In spite of this the patient grew worse; the respirations became Cheyne-Stokes in character; the temperature rose to 102.9°; and the patient died from respiratory failure. No abnormal ischaemia of the left fundus was noted on ophthalmoscopic examination. The blood pressure, however, did rise to 165/90 the day after the operation, suggesting cerebral ischaemia.

The autopsy (no. 10424) was performed by Dr. Margaret G. Smith. Nothing of significance was found outside the cranial cavity. The heart weighed 390 grams. The valves were all normal. The aorta showed some small fatty patches in its intima but was otherwise normal. The kidneys were normal.

On the left side of the brain was an area of softening occupying a part of the temporal lobe and a part of the parietal lobe. This softened area corresponded exactly to the distribution of the left middle cerebral artery. There was a hemorrhage in the meninges in the region of the Rolandic Fissure on this side. The most interesting condition, however, was that of the arteries at the base of the brain. On the right side there was a small aneurysmal sac measuring about 3 by 2 mm. The mouth of this sac opened into the middle cerebral artery very close to its origin from the carotid (Figs. 3 and 4). A very small branch, probably one of the anterior lateral ganglionic branches, opened from the middle cerebral artery just at the orifice of the aneurysmal sac. It was, therefore, difficult to determine whether the sac really arose from the middle cerebral or from this tiny branch. On the left side there was another sac apparently arising from a symmetrical position. This sac had ruptured, forming a false aneurysmal sac about 1 cm. in diameter. This had been broken into during the removal of the brain. It was possible to look into the sac towards its mouth and to see not only the opening into the middle cerebral artery but also another small opening which was the orifice of a small ganglionic branch. There had been a small hemorrhage from this sac. The left third nerve was flattened out on the surface of the sac.[4]

[4] The histology of the walls of such aneurysms is being studied in the Pathological Department and is to be the subject of a later communication.

The area of softening accounted for the terminal hemiplegia and death. It seemed probable that the softening could be attributed to an unfortunate combination of circumstances. The false aneurysmal sac was so situated that it pressed

FIG. 3. CASE 1. PHOTOGRAPH OF VESSELS OF CIRCLE OF WILLIS

on the middle cerebral artery. The pressure had apparently been insufficient to occlude this vessel until after the blood flow had been diminished by the operation. It was not the impression at the autopsy that the softening could have been due to the operative procedure without this complicating factor.

Case 2. M. G. H. No. N. M. 273205. E. M., a married housewife of 43, entered the Medical Service of the Massachusetts General Hospital on November 22, 1925, because of a severe headache of three weeks' duration.

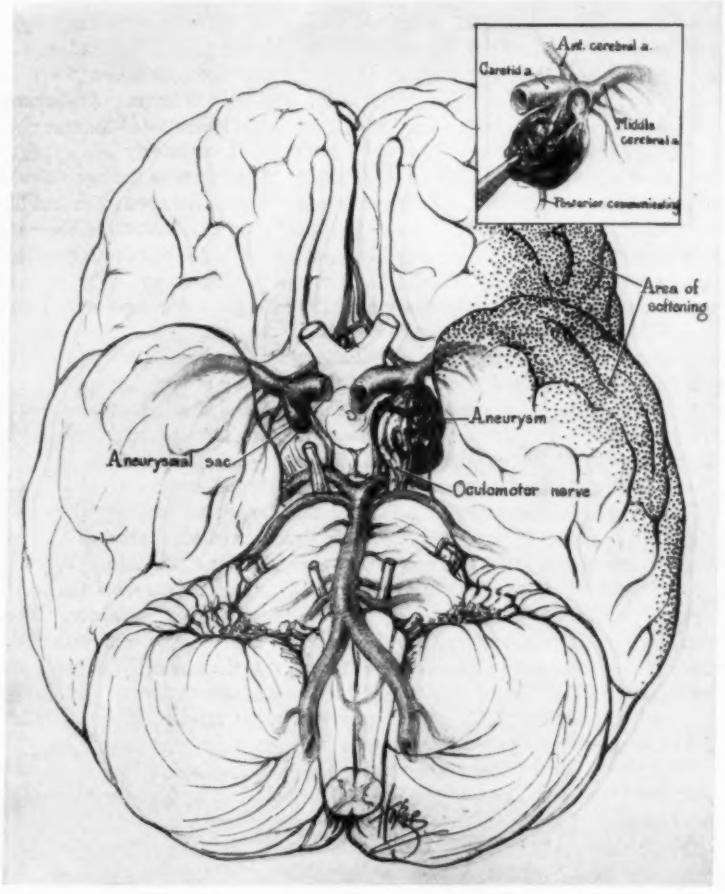

FIG. 4. CASE 1. DRAWING OF THE BASE OF THE BRAIN

The family history was entirely negative except that one sister had died of tuberculosis. The patient's husband and two children were living and well. She had had one still birth and one premature delivery. Since adolescence she

had had a tendency toward mild asthma, but this had troubled her very little during the preceding five years. Six years previously she had had a tonsillectomy, adenoidectomy, and a bilateral antrum operation because of her frequent sore throats and her asthma.

Three weeks before admission she felt nauseated in the morning on rising and later vomited. On the following day she complained of pain in the head, mainly right frontal and right supraorbital. On the third day after onset, the right eye became swollen and blue, and gradually closed within 48 hours. At the same time she felt numbness of the right side of the face and it was noted that the right corner of the mouth drooped down. The right pupil was widely dilated under the closed right upper lid. She had constantly a bad taste in her mouth. On the fourth day of her illness she was admitted to the Massachusetts Eye and Ear Infirmary where she remained 11 days. X-rays of the sinuses were taken there and found negative. Three teeth were said to need removal. The patient's condition remained about stationary while at the Eye and Ear Infirmary. She returned home and it is noted that she had supper with the family. She continued to have attacks of facial pain on the right side, especially the upper part. Three days before admission she became restless and had a generalized sharp intracranial pain similar to that which she experienced at the beginning of the illness. Six hours later she became unconscious; the eyes rolled up and the limbs became rigid. This seizure lasted five minutes. Following this she had a "terrific" pain in the back of the neck and over the middle of the back.

On examination she was mentally clear and oriented, but answered questions in a drowsy monotonous voice. She had a stiff neck and a bilateral Kernig's sign. The right eyelid was ptosed. There was a complete external and internal right ophthalmoplegia with anaesthesia of the right side of the face. The facial muscles on the right were slightly weak, especially around the corner of the mouth. General physical examination, otherwise, revealed nothing of significance. There were pyorrhea, bilateral conjunctivitis, emphysematous type of breathing (*cf.* history of asthma), and a third degree retroversion of the uterus. The blood pressure was 120/80. The pulse, temperature, and respirations were normal.

The impression on admission was aneurysm of the intracranial portion of the internal carotid artery with rupture and resulting subarachnoid hemorrhage.

Subsequent examinations strengthened this diagnosis. A lumbar puncture was performed and 10 cc. of xanthochromic fluid were removed, with an initial pressure of 205 mm. of water after 5 to 10 drops had been lost. The pressure after the removal of 10 cc. of fluid was 50 mm. The spinal fluid contained 20 red blood cells and 50 white cells per cubic millimeter. The white blood cells were equally divided between lymphocytes and polymorphonuclear leucocytes. The gold sol was 0001123221. The total protein in the spinal fluid was 216 mg. per 100 cc. The spinal fluid and blood Wassermann tests were negative. The blood non-protein nitrogen was 30 mgm. per 100 cc. The urine was not abnormal.

On November 27, five days after admission, it was noted that the patient had

fever (101° by rectum) for the first time. The fifth nerve pain was still very troublesome and the neck was becoming stiffer.

On December 5, the patient was mentally cloudy. A second lumbar puncture gave a result similar to the first except that the initial pressure was 260 mm.

On December 6 the patient went home much against the advice of the staff. Her condition was very much the same as at entry. Ligation of the carotid artery was under consideration.

Although a positive diagnosis cannot be made without an anatomical examination the symptomatology exhibited in this case is sufficiently characteristic, we believe, to warrant the probable diagnosis of aneurysm of the intracranial portion of the right internal carotid artery.

The twenty-nine cases from the literature are abstracted below.

Case 3. (Adams, James (4)). A sign-writer of 56 was first seen by Mr. James Adams, Assistant Surgeon to the London Hospital, on February 23, 1869. Six weeks previously he had developed giddiness and pain in the head, limited to a spot the size of a half crown in the right temporal region. After a few days the right eyelid had drooped and loss of motion of the globe and ulceration of the cornea had quickly followed. On examination the right eye was completely immobile and the pupil was fixed. The right cornea was insensible and ulcerated. The right eyelid was ptosed and edematous. There was complete anaesthesia of the right supra-orbital region, of the right side of the nose, and of the right supra-maxillary region. The patient died a month later with albuminuria, bronchitis and anasarca. At autopsy an aneurysm was found projecting from the right cavernous sinus, about the size of a walnut. It had not ruptured. This patient admitted having had primary syphilis in early life "but there was no evidence of there having been any secondary or tertiary periods." He was the father of a healthy family.

Case 4. (Beadles, Cecil F. (5)). A woman, aged 61, first came under the notice of Mr. Nettleship of St. Thomas's Hospital, on July 5, 1889. Her symptoms had started eighteen years previously with pain in the nose followed in a few weeks by drooping of the left upper eyelid and protrusion of the left eyeball. The left eye had become turned outward. Two and one-half years before first seen the patient had lost the power of swallowing, fluids returning through the nose. She had had several attacks of profuse bleeding through the left nostril. She had been deaf for five years. On examination in 1889, the left third and sixth nerves were completely paralysed, and possibly the left fourth. The left optic nerve was atrophied. There was doubtful slight exophthalmos on the left. The patient died on July 10, 1889 from a profuse left-sided epistaxis, while preparations were being made to tie the left common carotid artery. At autopsy an aneurysm of the cavernous portion of the left internal carotid artery 1½ inches in diameter was found. There was an irregular communication between it and the nasal pharynx.

The left optic nerve was displaced outwards, and the third nerve was pushed outwards and backwards. The fourth and sixth nerves were also displaced.

Case 5. (Beadles, Cecil F. (5)). A woman of 48 had been referred to Sir Victor Horsley for operation. The history is not available but she showed on examination external ophthalmoplegia on the right due to complete paralysis of the sixth nerve and partial paralysis of the third nerve. She had pain in the region supplied by the middle division of the V nerve. An exploratory operation was done and a pulsating tumor 1¾ inches in diameter was found. This originated from the right internal carotid artery immediately after that artery pierced the dura. The right common carotid was ligatured in the neck. Five years after the operation she was in good health.

Case 6. (Czermak (6)). A 59-year-old widow came first to the Clinic of Professor Czermak in Prague, in November 1900 for a beginning neuro-paralytic keratitis of the left eye. In 1894 she had developed an abducens paralysis on the left, and in 1898 a severe neuralgia over the distributions of the first and second branches of the fifth nerve on the left. In 1900 this region had become anaesthetic. At this time she showed tertiary syphilitic lesions of the skin and a diagnosis of gumma of the middle fossa was made. In January 1902 the third branch of the fifth nerve on the left, including its motor nerves, also became involved. On February 5, 1902, there was a sudden onset on the left of ptosis and complete paralysis of the third and fourth nerves. Shortly afterward the sight in the left eye was completely destroyed and the patient developed word-deafness. She died on February 12, of an apoplectiform seizure. At autopsy a ruptured aneurysm, the size of a mandarin, was found on the left internal carotid artery just where the ophthalmic artery is given off.

Case 7. (Davis, Loyal E., (7)). A married woman of 65 gave a history of attacks of pain of six weeks' duration. The pain had involved all three branches of the left fifth nerve. On examination the left pupil was larger than the right and was sluggish in its reactions. The left eyelid was ptosed and there was a paralysis of the extra-ocular muscles supplied by the left third nerve. The retinal veins in both eyes were dilated. The Wassermann tests of the blood and spinal fluid were negative. The patient had a sudden seizure and died within 12 hours. At autopsy there was a ruptured aneurysm the size of a pea on the outer coat of the left internal carotid artery where it turns forward to give off the middle cerebral and ophthalmic arteries.

Case 8. (Fearnsides, E. G., (8)). A married woman of 67 was admitted to the London Hospital February 11, 1913. In 1891, at the age of 45, after suffering for several years with chronic left-sided headache, she had had a seizure which had resulted in a right-sided hemiplegia and motor aphasia. She had completely

recovered from this attack. In June 1912 she had been at the Croydon Hospital complaining of ptosis of the left eyelid and supraorbital neuralgia. She had received an alcoholic injection for the neuralgia. On February 3 she had had a seizure in which consciousness was lost and the following day she had again become aphasic. On admission she was dazed and drowsy. The left third nerve was completely paralysed. The left fourth and sixth nerves were not affected. The tissues around the left orbit were edematous. She had two more seizures, on February 13 and February 15th. She died on February 21st. At autopsy a ruptured and partially thrombosed aneurysm, 3 cm. in diameter, was found on the left middle cerebral artery near the base of the brain. The left third cranial nerve was small and grey in color. The cerebral vessels generally were atheromatous, as was the aorta.

Case 9. (Fearnsides, E. G., (8)). An unmarried grocer of 40 was admitted to the London Hospital on January 16, 1908. Twenty days previous to admission, while at stool, he had been seized with a pain shooting down his back into his legs. He had then become dizzy and had vomited. He had developed a severe headache. The following day there had appeared weakness of his left leg and 13 days later ptosis of the right eyelid. On January 11, he had had a second seizure. Examination on admission showed absent knee-jerks and ankle-jerks, an extensor plantar response on the left, and complete paralysis of the third and fourth nerves on the right. The sixth nerve was not affected. Lumbar puncture showed a bloody spinal fluid under increased pressure. The urine contained considerable albumin and rare hyalin casts. Later during his stay in the hospital the knee-jerks and ankle-jerks were obtained but varied from time to time. On January 30, he had a third seizure associated wtth frontal headache and tenderness of the scalp. Kernig's sign became positive on the right. He died February 1. At autopsy a small ruptured aneurysm, the size of a haricot bean, was found on the right carotid artery close to the origin of the middle cerebral artery. No atheromatous lesions were present on the cerebral vessels.

Case 10. (Fearnsides, E. G., (8)). An unmarried painter of 19 entered the London Hospital on June 8, 1911. While at work on June 1 he had been suddenly seized with severe headache "as if the head would burst" and "a feeling of stiffness down the left side of the neck." Later he had vomited but had not lost consciousness. The headache had persisted in the left supraorbital region and on June 5 he had been unable to open his left eye. On examination on June 8, the left side of his head was tender on pressure. The left third and fourth nerves were paralysed. The sixth nerve was not affected. The neck was drawn to the left by spasm of the muscles on that side. The urine was negative. Lumbar punctures on June 15 and June 18 showed blood. The fundus on the left presented a hazy disc and dilated veins. On June 24, it is noted that Kernig's sign was still present in both legs. He died that day. At autopsy an aneurysm (1.5 cm. by

1 cm.) was found at the junction of the left internal carotid and left posterior communicating arteries. This had ruptured. The left third nerve was stretched over and adherent to the posterior extremity of the aneurysm. There was no other evidence of cardio-vascular disease.

Case 11. (France, John F., (9)). A servant girl of 20 was admitted to Guy's Hospital on May 13, 1846 because of ptosis of the right eyelid. For a month she had suffered from headache and giddiness. Five days before admission she had been suddenly seized with pain in the head over the right eyebrow, accompanied by faintness and vomiting. The next morning she had developed ptosis of the right eyelid. Examination on admission showed ptosis of the right eyelid, difficulty in adduction, elevation, and depression of the right globe, and a dilated right pupil which reacted only slightly. Abduction of the right eye was perfect. The headache continued. On May 31 she died suddenly. At autopsy a "hemorrhage had taken place from the posterior communicating artery of the carotid of the right side, through the parietes of which was an aperture, overlaid by a circumscribed clot (termed by some an aneurysm) of about the size of a large pea. Under this the right nerve of the third pair was spread out, having obviously undergone a degree of compression, by this older effusion, more than sufficient to explain the arrested functions of the nerve." The autopsy was otherwise negative.

Case 12. (Hare's Case, reported by William Gull (10)). A woman, 18 years old, had had a severe headache and symptoms of acute mania two years before death. She had recovered from this after several months, but continued to have pains in the head with occasional vomiting. For one week she had had ptosis of the left eyelid. On examination, besides the ptosis, the left eye was abducted and the pupil was large. There were shooting pains in her left temple. She had a sudden seizure and died within ten minutes. At autopsy there was a ruptured aneurysm the size of a filbert on the left posterior communicating artery.

Case 13. (Harris, George B., (11)). A negress, aged 39, was admitted in coma to the neurologic service of Cook County Hospital on February 23, 1925. The patient had had a cervico-occipital headache for two weeks. There had also been a history of dizzy and fainting spells. On the morning of admission she had been found in bed unconscious. On examination the eyelids were drooping. The left pupil was large and fixed. There was no Kernig's sign. The spinal fluid showed marked xanthochromia, a positive benzidine test, and a negative Wassermann reaction. The blood Wassermann was positive. She died ten hours after admission. At autopsy a small ruptured aneurysm was found at the juncture of the internal carotid and the posterior communicating arteries. The heart and kidneys were normal.

Case 14. (Holmes, T., (12)). A boy, aged 16, was admitted to St. George's Hospital on August 21, 1860, because of heart disease. He complained of headache

and pain over his left eye which had come on four days before admission. On examination he had definite evidence of mitral disease. On August 24, he complained of giddiness. On the following day there was a tendency to ptosis on the left side. By a little more than a fortnight the ptosis has become complete. Examination then showed on the left a dilated and fixed pupil, a fixed eyeball, and numbness over the distribution of the first branch of the fifth nerve. The eye condition subsequently improved, but he died on November 8 from cardiac failure. At autopsy there was a fresh endocarditis. There was an aneurysm arising from the cavernous portion of the left internal carotid artery about the size of a small nut. The third nerve was tightly stretched over the tumor, and the fourth nerve and ophthalmic branch of the fifth nerve had likewise been pressed upon by the aneurysm.

Case 15. (Peacock, Thomas B., (13)). A man aged 34 was admitted to St. Thomas's Hospital, October 30, 1875. He had fractured his skull 8 years previously. After the accident he had been subject to pain in the right parietal region. On the morning of admission he had had a severe headache and had felt very ill. On admission he was dull and later had a fit and became unconscious. On examination on October 31, his head was drawn to the left side by rigidity of the muscles on that side. The left eyelid was entirely ptosed. The left pupil was markedly dilated and the eye was everted. The right side of the face was motionless. He died that night. At autopsy a ruptured aneurysm, the size of a small marble, lay immediately at the outer side of the termination of the left internal carotid artery and arose from the left middle cerebral artery close to its origin. The third nerve, where it passed beneath the tumor, was flattened, of a yellowish color, and softened. There was an adherent pericardium without valvular disease. The internal carotid arteries were atheromatous. There was an irregularity of the petrous portion of the temporal bone, probably the result of the fracture. The kidneys were granular with adherent capsules.

Case 16. (Hutchinson, Jonathan, (14)). A married woman of 40 first came under the observation of Dr. Jonathan Hutchinson at the Moorfields Ophthalmic Hospital on March 8, 1861. For one year previous to this she had suffered from drooping of the left eyelid, and a coincident aggravation of her habitual headaches. The headaches, which she had had for 10 years, had been throbbing and frontal. Examination revealed internal ophthalmoplegia on the left, weakness of all muscles supplied by the left third nerve, and complete paralysis of the left sixth nerve. The fourth nerve was not affected. Later it was noted that sensation was impaired in the left supraorbital region. Several months later the paralysis of the left third nerve became complete. A sensation of numbness in the left cheek also appeared. A bruit was heard. Ligature of the carotid artery was advised and refused. From that time on there was little change in her cerebral condition until her death, in 1872, from abdominal aneurysm. At autopsy a solid

aneurysmal tumor the size of a bantam's egg was found originating from the left internal carotid artery. The tumor rested on the Gasserian ganglion. The motor nerves of the eye ball were lost in the wall of the tumor.

Case 17. (Kirby, D. B., (15)). A man aged 60, sought relief on January 2, 1923, at the New York Eye and Ear Infirmary for severe pain in and about the right eye. Thirty-four years previously he had fractured his skull. At that time he had developed immobility of the right eye, ptosis of the right upper eyelid, and deafness in the right ear. There had been no other symptoms until December 1922 when, after a drinking bout, he had begun to have a stabbing pain in and about the right eye. On examination he had complete paralysis of the third, fourth, and sixth nerves on the right, and anaesthesia in the region supplied by the upper two branches of the fifth nerve on the right. In February 1923, this pain suddenly ceased. Subsequent examination in February at the Bellevue Hospital showed, on the right, nerve deafness, diminished visual acuity, an irregularly contracted visual field, and a slightly pale disc. X-ray showed a mass in the right middle cranial fossa eroding the sella and the floor of the middle fossa. The patient died March 28, 1923, from some form of anemia. At autopsy there was a large aneurysm (1×3 cm.) of the right internal carotid artery almost entirely organized, with a small area of organizing and fresh blood clots. The right optic tract ran up and over the inner surface of the mass. The third, fourth, and sixth nerves had been destroyed by pressure.

Case 18. (Magnus, Vilhelm, (16)). The patient, aged 69, first consulted Dr. Vilhelm Magnus of Oslo, Norway on March 23, 1924, because of pain in the crown of the head which radiated down the right part of the forehead, the right eye and the right side of the nose toward the right ear and down the right lower jaw. Six years before he had been treated at the Rikshospitalet for a right abducens paralysis. The pain had begun three months before. On examination the right palpebral fissure was smaller than the left. The right eye was turned inward. The right corneal reflex was absent and there was hypesthesia throughout the right side of the face. The eye signs were attributed to a paralysis of the right sixth nerve and the sympathetic nerve. Blood Wassermann negative. On April 8, 1924, an operation was attempted to remove the trigeminus root. A tumor the size of a chestnut was found situated on the surface of the Gasserian ganglion. In the attempt to remove this there was a gush of blood which was only stopped by rapid ligation of the internal carotid artery in the neck. The trigeminus root was then removed. The patient made an uneventful convalescence except that his left hand became paralyzed three days after the operation. He was discharged April 23, 1924, entirely relieved of his pain.

Case 19. (Packard, Maurice, and Zabriski, E. G., (17)). A man, aged 21, entered the Neurological Institute, New York City, on December 29, 1917. Six-

teen days previous to admission, while fixing the furnace, he had felt a sudden sharp pain across the eyes, radiating over the top of his head. He soon had become dizzy and unconscious. The following day he had regained consciousness and had complained of headache and diplopia. At that time he had had a stiff neck, a positive Kernig's sign, and 30 cc. of bloody cerebro-spinal fluid had been withdrawn. On December 26, he had had a second seizure. On admission there were no localizing signs. Neither ankle-jerk could be obtained. Three days later the right pupil became dilated and fixed, and the left knee-jerk was exaggerated. That night he had a convulsion involving the left arm, left leg, and both sides of the face. On January 4, the right palpebral fissure had become narrowed. The pupil was still dilated and fixed. The right disc was choked. The nasal field of the right eye was obliterated. On January 4, Dr. Elsberg performed a right subtemporal decompression. A subdural hemorrhage was found. The patient died that night. At autopsy a ruptured aneurysm the size of a cherry was found on the right middle cerebral artery, infringing on the right optic nerve anteriorly to the chiasm.

Case 20. (Parker, H., L. (18)). A man, aged 21, came to the Mayo Clinic September 13, 1925, complaining of double vision and numbness of the right side of the face. Two years before he had been knocked unconscious for fifteen minutes but there had been no sequelae. Fourteen months before admission he suddenly had developed diplopia, which had been more marked on looking to the right. Three weeks before admission he had suffered from severe bilateral frontal headaches for two or three days and thereafter had noticed that the right side of his face was numb. Later his jaw muscles on the right side had become weak. He had had projectile vomiting for three or four days before admission. On examination there was apparently a congenitally anomalous development of the whole left side of the body. The arm and leg on the left were larger than on the right side and the skin on the left side of the body was cyanotic with enlarged venules. The right sixth nerve was completely paralysed and the right side of the face was markedly hyperaesthetic. The muscles of mastication on the right were almost completely paralysed. Oppenheim's and Gordon's signs were positive on the left. The spinal fluid was xanthochromic. Soon the right third and fourth nerves became completely paralysed, and still later the right seventh nerve. On September 20 he became suddenly worse and the neck became rigid. Spinal fluid now contained red blood cells. He died suddenly on September 26. At autopsy a ruptured saccular aneurysm of the right internal carotid artery in its course in the cavernous sinus was found. There was also a fusiform aneurysm of the left internal carotid artery in the carotid canal and an anomalous arrangement of the circle of Willis.

Case 21. (Pitt, Newton, (19)). A man, aged 66, had as his chief symptom, besides general ill health, ptosis. He had old kidney disease and died with suppu-

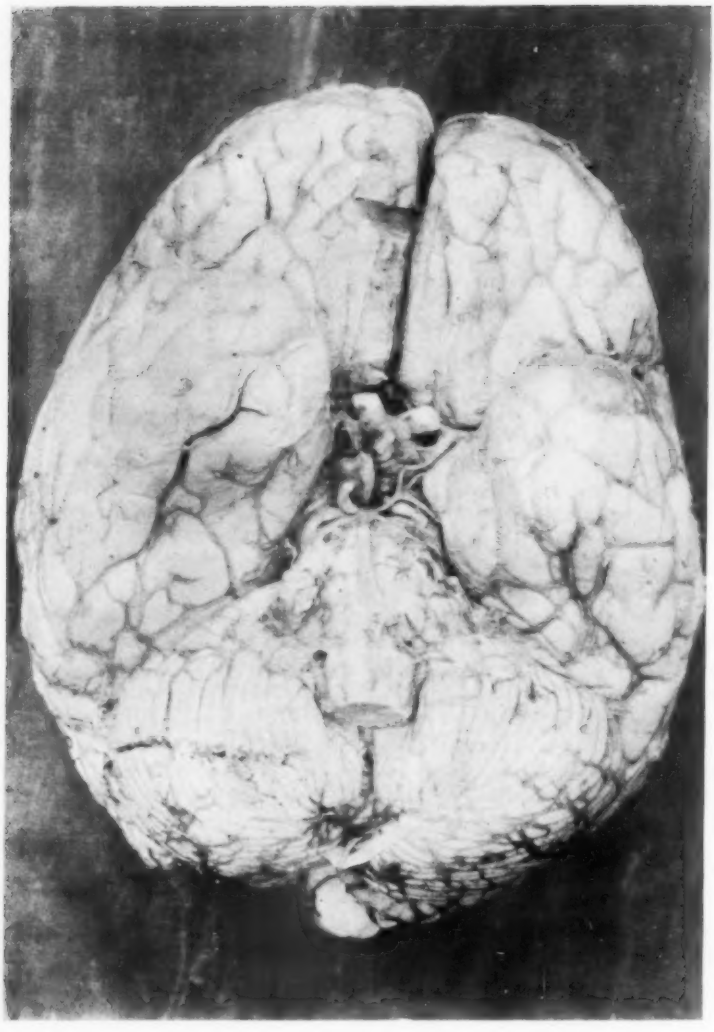

FIG. 5. CASE 22. ANEURYSM ON THE RIGHT POSTERIOR COMMUNICATING ARTERY. (AFTER SANDS)

rative nephritis. At autopsy a fusiform aneurysm of the internal carotid artery was found pressing on the third nerve. The aneurysm measured 2 by 1 cm.

Case 22. (Sands, Irving, J., (20)). (See Fig. 5). A married woman of 34 entered the Brooklyn Jewish Hospital on November 25, 1925. Since November 7, she had had headaches, pain in the back, diplopia, and ptosis of the right eyelid. She had had her teeth extracted without relief. On November 25, her husband had found her unconscious in bed. She had been taken directly then to the hospital. On admission there was complete paralysis of right third nerve, absence of the right corneal reflex, paralysis of the left side of the body, left ankle clonus, and left Babinski sign. The right sixth nerve was not affected. She remained unconscious until November 27. A lumbar puncture then showed bloody spinal fluid under increased pressure. The blood and spinal fluid Wassermann were negative. The eye-grounds showed moderate arteriosclerosis. She continued to improve until December 2, when she had a second seizure. Cervical rigidity was noted. She died December 4. At autopsy a ruptured aneurysm was found on the right posterior communicating artery of the circle of Willis. The right third nerve was somewhat thinner than the left, was yellowish in color, and was pressed upon by the aneurysm.

Case 23. (Shaw, B. Henry, (21)). A woman of 50 came under treatment at the County Asylum, Stafford, England, on August 15, 1900. For two years she had been suffering from auditory hallucinations. A few years before admission she had developed a violent pain in the right side of her head, and twenty-four hours later had developed paresis of the right third nerve. Since then she had had a constant buzzing in the right side of her head and periodic acute pain of a hemicranial nature. On examination she showed "almost complete right ophthalmoplegia, *viz.*, ptosis, external strabismus, and fixity of pupil." On February 19, 1901, she died suddenly from an apoplectic seizure. The convulsions were strongest on the left side. At autopsy there was a ruptured sacculated aneurysm, the size of a pea, on the right middle cerebral artery. There was also a sacculated aneurysm, about the size of a walnut, of the right internal carotid just as it pierced the dura. The heart was enlarged and the aorta, cranial and other arteries were markedly atheromatous.

Case 24. (Smith, R. W., (22)). A man, aged 33, was admitted to the South Union Hospital in 1850 in coma. He had been very much overworked and, following a debauch, he had been found insensible and had been brought to the hospital. He recovered from the attack but continued listless. He had also ptosis of the right eyelid, an external squint, and impairment of vision in the right eye. The condition remained unchanged until four years later when he had another cerebral attack and died. At autopsy there was found a ruptured aneurysm the size of a small plum at the termination of the internal carotid artery. The third nerve

had become amalgamated with the tumor and had lost its natural color. The optic nerve was "soft and flabby and of dingy color."

Case 25. (Symonds, C. P., (1)). (See Fig. 6). A married woman of 52 entered the Peter Bent Brigham Hospital on August 30, 1920, complaining of headache and vomiting. For seven years she had suffered from shortness of breath, attributed to high blood pressure. In April 1919 she had had "influenza" and

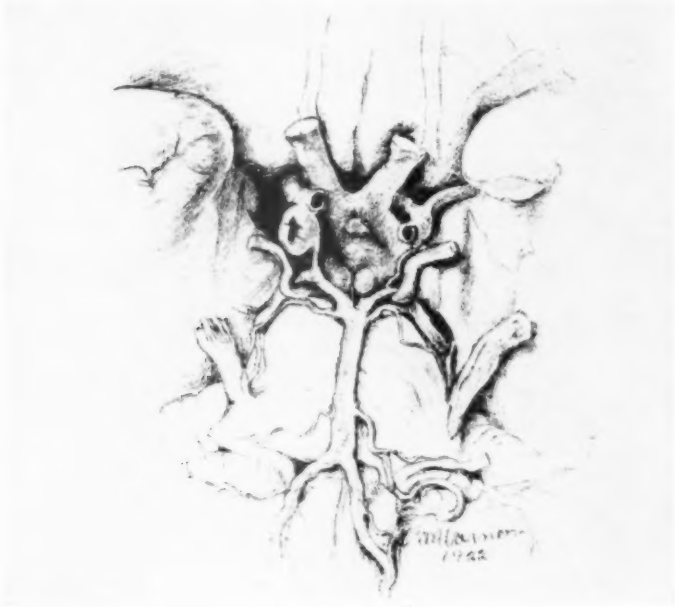

FIG. 6. CASE 25. DRAWING OF THE BASE OF THE BRAIN SHOWING THE ANEURYSM AT THE JUNCTION OF THE RIGHT INTERNAL CAROTID AND POSTERIOR COMMUNICATING ARTERIES. (AFTER SYMONDS)

associated with it pain in the back of the neck radiating down into her back, and vomiting. For a while after that her gait had been unsteady. Since then she had suffered from attacks of severe right frontal headaches. In December 1919 she had noticed diplopia. On August 14, 1920, she had been seized with a sudden severe pain in the supra-orbital region and vomiting. A few days later her right eyelid had drooped and there had developed slight exophthalmos on the right. On examination she showed bilateral engorgement of the retinal veins, slight bilat-

eral exophthalmos especially on the right, complete paralysis of the third and fourth nerves on the right, and nerve deafness on the right. Urine negative. Blood Wassermann negative. On September 2, she suddenly became very much worse. Retinal hemorrhages were noted in both fundi. A subtemporal decompression on September 3 revealed a tense dura beneath which was recently clotted blood. She died on September 4. At autopsy there was a small saccular aneurysm about 8 mm. in circumference at the junction of the right internal carotid and the posterior communicating arteries. This had ruptured. Extravasated blood was found in the arachnoid sheaths of both optic nerves (*cf.* retinal hemorrhages). The right third nerve opposite the sac was thinned and showed a greyish-yellow color instead of the normal clean pallor. The cerebral vessels were markedly atheromatous.

Case 26. (Viets, Henry, (23)). A single girl of 26 entered the Peter Bent Brigham Hospital March 15, 1927 complaining of headache, numbness over the right eye, and drooping of the right eyelid. The onset had occurred seven weeks previously with a throbbing headache in the right frontal and occipital region. A few days later the right eye had closed and numbness and pain had been noted around the right eye, the right side of the nose, and part of the right cheek. On admission there was ptosis of the right eye-lid, complete external and internal ophthalmoplegia on the right, loss of corneal reflex on the right, and disordered sensation in the right supraorbital region. Spinal fluid examination negative. Urine negative. Blood Wassermann negative. Condition remained unchanged until April 19, 1917 when an exploratory operation was performed by Dr. Harvey Cushing. A pulsating tumor the size of a walnut was found. It was thought to have originated from the internal carotid artery. The condition was not interfered with and the patient made an uneventful convalescence. She died suddenly a year later. There was no autopsy.

Case 27. (White, Hale, (24)). A woman of 34 was admitted to Guy's Hospital, December 29, 1893. She had always been subject to severe headaches. On December 25, while at dinner, she had suddenly fallen off her chair unconscious. She had regained consciousness after 8 minutes but had had an intense headache, and violent vomiting had set in. On admission she had a severe headache with photophobia. She could not bear the weight of an icebag on her head. On the following day her head was retracted and she had pain running down the spine to the sacrum. There was some blurring of the left disc. On January 2, there was slight right facial paralysis. Diplopia was noted. The headache was noted as being most intense in the left temporal region. On January 3, ptosis of the left eyelid became marked and the next day there was slight left external strabismus. On January 7 the left third nerve paralysis was complete. On January 18, after several days of unconsciousness, she died. At autopsy a ruptured aneurysm ($\frac{3}{4}$ by $\frac{1}{2}$ inch) springing from the left internal carotid just before its bifurcation was

found. The aneurysm had pressed on the left third nerve. Its wall had two patches of atheroma in it.

Case 28. (Wichern, Heinrich, (25)). A man aged 32, was brought unconscious to the Medical Clinic of the Leipsic University. At the age of 10 he had suddenly developed a right-sided hemiplegia. Following this he had had no trouble until the day of admission when after some excitement he had become unconscious. On admission there was a right-sided paralysis. Later he recovered consciousness but had difficulty in speaking. Six months later he developed a left-sided oculomotor paralysis. One year later, at the age of 32, he had a third seizure and died soon afterward. At autopsy there were old and new hemorrhages over the left side of the brain and an aneurysm the size of a cherry in the left fossa of Sylvius.

Case 29.[5] (Woltman, H. W., and Shelden, W. D., (26)). (See Fig. 7). A strong active boy, aged 20, whose only complaint has been occasional attacks of dizziness was registered at the Mayo Clinic, May 3, 1925. Five weeks before he had pushed a motor cycle through a mile of sand; had called at a farmhouse for some fuel; and, while chatting with the proprietor, had suddenly fallen to the ground. He had immediately regained his feet and had ridden home. Two weeks before admission, while playing ball, he had been stricken with severe pain in the occiput and had become dizzy. Later he had vomited and had manifested marked photophobia. Two days before admission he had suddenly sat up and screamed because of severe pain in the back of his neck. On admission there was generalized rigidity. The left pupil was larger than the right. There were several massive hemorrhages of both retinas and discs. The spinal fluid was bloody. On May 8 left ptosis appeared. On May 9 it was noted that he did not move the right side of his body. The left pupil became large and fixed. The discs were choked. He died May 12. At autopsy a ruptured aneurysm was found at the juncture of the left posterior communicating and middle cerebral arteries. The aneurysm extended backward under the third nerve which was raised from its bed and stretched over it. There was a second smaller aneurysm at the juncture of the anterior communicating and anterior cerebral arteries. There was a coarctation of the aorta, which had been observed clinically, and foetal lobulations in the kidneys.

Case 30. (von Jaksch (27)). A twenty-five year old teacher was admitted to the Clinic of von Jaksch in Prague on April 24, 1918, in deep coma. For several weeks she had had severe headaches. On April 22 she had vomited. On April 23 there had developed severe pain in the back of the neck and nausea. On the day of admission she had cried "Mother, my eyes" and had sunk into coma. On

[5] Case also reported by Parker (18) Case 2.

examination there was a complete external and internal ophthalmoplegia on the right, a slight facial weakness on the right, slight ptosis of the left eyelid, external strabismus of the left eye, hemorrhages in both fundi, and a stiff neck. The spinal fluid was bloody and under increased pressure. The Wassermann test

FIG. 7. CASE 29. RUPTURED ANEURYSM AT JUNCTURE OF THE LEFT POSTERIOR COMMUNICATING AND MIDDLE CEREBRAL ARTERIES. AN UNRUPTURED ANEURYSM AT THE JUNCTURE OF THE ANTERIOR COMMUNICATING AND ANTERIOR CEREBRAL ARTERIES

(After Woltman and Shelden)

was negative. The urine showed a small amount of sugar and a trace of albumin. On April 25 she recovered consciousness. A left hemiplegia was noted at that time. On April 29 she sank into coma and died. At autopsy there was a ruptured aneurysm, the size of a nut, arising from the right posterior communicating artery near the posterior cerebral artery. The heart was essentially normal.

Case 31. Reinhardt (28)). The patient was a forty-one year old man who was treated in the Laryngological Clinic of Dr. Spiess in Leipsic. When first seen in 1904 he had had paralysis of his ocular muscles on the left for one year. For

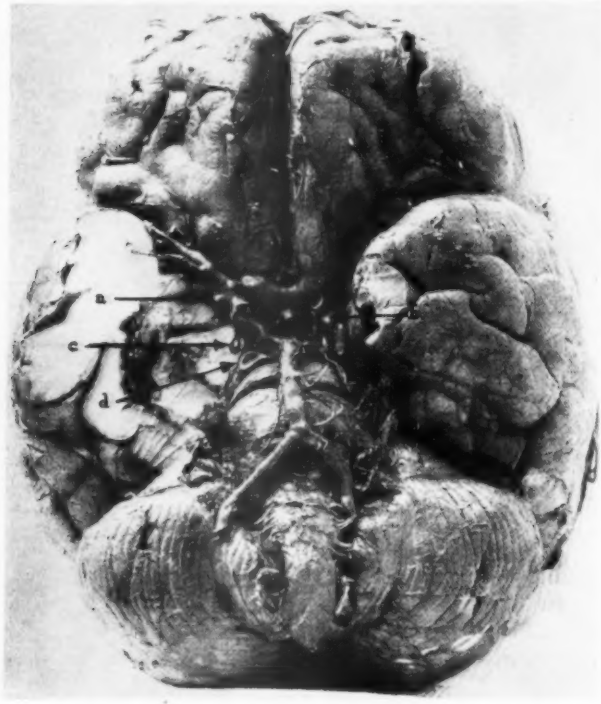

FIG 8. CASE 32

A. Aneurysm on right internal carotid artery.

B. Aneurysm on left internal carotid artery.

C. Aneurysm on right posterior communicating artery (ruptured) after removal from depression in third nerve.

D. Depression in right third nerve. (After McCordock).

four weeks he had had left-sided headaches. On examination he showed a complete ophthalmoplegia. In 1906 he suffered from severe headaches in his left forehead and left eye. Exophthalmos of the left eye was noted at that time. He lost the sight in his left eye and the left seventh nerve became paralysed. An

X-ray taken in 1912 showed an obliteration of the sella turcica and of the left sphenoidal sinus. In January 1913 the left maxillary sinus was opened and a pulsating tumor was found in place of the ethmoid bone. The tumor was incised and he died shortly afterwards from severe hemorrhages. At autopsy there was a large aneurysm of the left internal carotid artery with compression of the brain, cranial nerves, and hypophysis, and destruction of the base of the skull.

Case 32. (McCordock (37)). (See Fig. 8). The patient was a woman, 55 years of age, a known diabetic, who was admitted to the Buffalo General Hospital in September 1923 because of severe pain in the right side of her face. She had had a similar attack of pain two weeks previously associated with vomiting. Thirty-six hours after the onset of the second attack, she had developed ptosis of her right eyelid and a dilated and fixed right pupil. On examination she showed peripheral arteriosclerosis with a slightly enlarged heart and a blood pressure of 175/110. There was a complete paralysis of the right third nerve and a partial one of the left third nerve. On the third day after admission she suddenly died. A lumbar puncture, performed shortly before death, revealed a bloody spinal fluid. At autopsy there was extreme arteriosclerosis of the vessels at the base of the brain. There was a ruptured, pea-sized aneurysm on the right posterior communicating artery near its junction with the internal carotid artery. The aneurysm pressed upon the third nerve. There were similar unruptured aneurysms on the basilar and left internal carotid arteries.

DISCUSSION

In selecting this series I have taken only those cases of aneurysm which occurred in close proximity to the juncture of the internal carotid artery with the circle of Willis. This includes those on the intracranial portion of the internal carotid artery, those on the anterior part of the posterior communicating artery, those on the very proximal end of the middle cerebral artery, and those at the junction of these vessels. No cases were accepted which did not give symptoms before death on which a correct diagnosis might at least have been suspected. From the literature I have accepted only cases which have been confirmed by autopsy or operation. Cases of arterio-venous aneurysm with pulsating exophthalmos have not been included. There are at least two reasons why my group should be segregated from the more general class of intracranial aneurysms. In the first place the clinical picture is extraordinarily constant, and in the second place the condition is so closely allied with arterio-venous aneurysms occurring in the cavernous sinus that one is led to hope that therapeu-

tic procedures which have been helpful there may likewise be effective in certain cases from this group.

ETIOLOGY

Inasmuch as I have been particularly interested in the diagnosis and clinical syndrome, I have not confined my series to cases belonging in any one etiological group. This series comprises at least five etiological groups, *viz.*

(i) Mycotic aneurysms from infective emboli (*cf.* Case 14).

(ii) Post-traumatic aneurysms resulting from fracture at the base of the skull (*cf.* Cases 15, 17).

(iii) Aneurysms due to syphilis (*cf.* Cases 3, 6, 16, and possibly 13, 24, and 31).

(iv) Aneurysms associated with and probably due to atheromatous changes in the vessels (*cf.* Cases 8, 18, 21, 23, 32 and possibly Cases 4, 5, 7, 25, and 27). It is of course impossible, often, to be sure whether an aneurysm in an elderly person with atheromatous lesions on the cerebral vessels is due to arteriosclerosis or whether the arteriosclerosis is merely contributory or even incidental. In case 25, for instance, the aneurysm resembles in many ways the congenital type (*v. infra*) but cannot be unreservedly classified as such because of the presence of atheromata. It is possible in these cases that a congenital weakness becomes manifest in the form of an aneurysm only where there is the additional factor of arteriosclerosis.

(v) Aneurysm resulting from congenital defects in the walls of the cerebral vessels (*cf.* Cases 1, 2, 9, 10, 11, 12, 19, 20, 22, 26, 28, 29, 30, and possibly 25 and 27).

The last of these groups is the largest and most interesting. The aneurysms are thought to be due to congenital defects in the medial wall of the artery (8) (28) (30), as pointed out first by Eppinger (30). They usually occur where the vessel divides or where a small branch is given off. Symptoms usually come on in young adult life (ages 18, 19, 20, 20, 21, 25, 26, 32, 33, 34, 34, 40 and 43 in our series). As in cases 1, 20, 29, and 32, the aneurysms are often multiple (see also Green (29) Case III; Fearnsides (8) Cases 3, 4, 11, 26). There may be evidence of congenital abnormalities elsewhere. Thus, in case 3 the patient had a congenitally deformed hand and in case 20 the

patient had an abnormal development of the whole left side of his body. Coarctation of the aorta may be found. (Case 29; see also Green (29) Case 3; Weber (31)).

SYMPTOMS AND SIGNS

One cannot read over these case histories without being struck with the marked similarity in the clinical pictures which these cases present. The signs and symptoms group themselves into two main headings:

(a) What Symonds (1) termed the "neighborhood signs" dependent on pressure by the aneurysm on the particular structures in this locality.

(b) Signs and symptoms due to leakage from the aneurysm.

A consideration of the anatomy of this region shows that an aneurysmal tumor might involve many structures. Many of the aneurysms, in fact probably almost all the congenital ones, are too small before leakage to cause localizing signs and symptoms. After leakage the localizing signs and symptoms do not usually appear immediately, but may be delayed three to twenty days (Cases 1, 2, 9, 10, 19, 20, 25, 27, 29, 32). The explanation of this latent period is probably shown in case 1 as well in other cases. It would appear that the leakage from the aneurysm tends to form a false aneurysm much larger than the original one and that this in turn causes pressure on the surrounding structures (See plate IV). Thus, whereas the neighborhood signs and symptoms will be similar, the sequence of events will vary depending on whether these signs and symptoms occurred before leakage, as in the larger aneurysms (Cases 3, 4, 5, 6, 14, 16, 17, 18, 23, 24, 26, 31), or after leakage, as in the smaller ones (Cases 1, 2, 8, 9, 10, 11, 12, 13, 15, 20, 25, 27, 29, 30, 32). The neighborhood signs were well summed up in 1872 by Bartholow (32). "An aneurysm of the internal carotid will affect the sense of smell by compression of the olfactory nerve; will also cause ptosis, convergent strabismus, and a dilated pupil by pressure on the motor oculi; will produce amaurosis by direct interference with the optic; will cause congestion of the eye and swelling of the veins of the face by compression of the cavernous sinus; and will be accompanied by intense tic douloureux, especially in the ophthalmic division due to irritation of the fifth nerve. With

the growth of the tumor, especially if that part of the artery within the carotid canal be involved, there will occur noises, pulsating in character, in the ear, followed by impaired hearing, and finally by complete deafness. The facial nerve may also become involved, and paralysis of the face on the same side will be observed. Softening of the neighboring part of the middle lobe will take place, and by reason of this, or by pressure on the crus cerebri, crossed hemiplegia will occur."

The olfactory nerve was not noted as being involved in my series. The third nerve was involved in every case. In most cases the third nerve paralysis was both external and internal. Case 18 was unusual in that the sympathetic fibers were involved. The fourth nerve was frequently paralyzed but quite often escaped, as in Case 1. In many of the reported cases it was impossible to tell from the data given whether the fourth nerve was involved or not. It is quite surprising how often the sixth nerve escaped injury (Cases 1, 8, 9, 10, 11, 12, 15, 23, 24, 25, 27, 28). In Cases 2, 6, 17, 19, 24 and 31, the optic nerve was involved by direct pressure. In Case 19 this pressure was on the lateral aspect of the nerve causing nasal blindness in the corresponding visual field. Signs of pressure on the cavernous sinus were not infrequent. Thus, edema of the eyelid was noted in Cases 2, 3 and 8, exophthalmos in Cases 2, 10, 19, 25, 27, 29. Next to the third nerve the ophthalmic branch of the fifth nerve was most frequently involved. This usually took the form of pain over the area supplied by this nerve (Cases 1, 2, 3, 6, 8, 9, 10, 11, 12, 14, 16, 18, 23, 25, 26, 27, 30, 31, 32). In some cases there was decreased sensation in this area and often an absent corneal reflex (Cases 2, 3, 6, 14, 16, 17, 18, 20, 22 and 26). Occasionally hyperaesthesia and photophobia were noted (cf. Cases 25, 29). Other branches of the fifth nerve, including sometimes the motor branch, were involved by the more extensive lesions (Cases 5, 6, 7, 16, 17, 18 and 20). Because of this involvement of the fifth nerve the condition is often diagnosed and treated as migraine. Cushing (33) described a case diagnosed as ophthalmoplegic migraine which in retrospect he thought probably represented this condition. It is of interest that the description of ophthalmoplegic migraine given in The Oxford System of Medicine (34) suggests that this syndrome may be often due to repeated leakages from a small aneurysm. The audi-

tory nerve was involved in Cases 4 and 25 and the facial nerve in Cases 2, 20, 27 and 31. Frequently after leakage, especially with aneurysms at the lower end of the middle cerebral artery, there may be involvement of the brain cortex as shown by a crossed hemiplegia, or an aphasia if the lesion be on the left (Cases 8, 9, 15, 20, 22, 23, 28, 29 and 30).

The neighborhood signs, of course, merely give an indication as to the location of the tumor. Unless there is in addition evidence of one or more episodes of leakage of blood into the subarachnoid spaces one could not arrive at more than a tentative diagnosis. The criteria for the diagnosis of a subarachnoid hemorrhage have been clearly discussed by Symonds (2). In my series, Cases 1, 2, 8, 9, 10, 11, 13, 15, 19, 20, 22, 27, 29, 30 and 32 gave clinical evidence of leakage.

As might be expected, the onset is usually sudden and comes during exertion (Cases 1, 9, 10, 19, 29). The patient is almost invariably seized with a headache, very often becomes giddy or unconscious for a while and usually vomits within the first few hours. He may, of course, quickly succumb. These first symptoms are due to increased intracranial pressure. Later there develop signs and symptoms due to the irritation set up by the blood in the subarachnoid spaces. These are pain in the back of the neck, often running down into the back, stiff neck, and Kernig's sign. In Cases 10 and 15, it is interesting that the stiff neck was confined to the side of the lesion, suggesting that the hemorrhage remained localized on that side. Spinal puncture, if performed, quickly confirms the diagnosis. The fluid is under increased pressure and uniformly bloody if the hemorrhage has been recent (Cases 2, 9, 10, 19, 20, 22, 29, 30, and 32); and, if the hemorrhage has occurred some time previously, the spinal fluid is xanthochromic (Cases 2, 13, and 20). Symonds (2) has pointed out that lumbar puncture is not always a safe procedure because of the danger of starting the hemorrhage afresh by release of pressure. In Case 1 lumbar puncture was withheld for this reason on the day before operation. Retinal hemorrhages have been present in several cases of subarachnoid hemorrhage at the base of the brain (*cf.* Cases 25, 29, and 30). This was shown by Doubler and Marlow (35) to be due to a marked distention of the optic nerve sheaths with blood. There is usually a slight fever for several days following the hemorrhage.

Transient massive albuminurias have been described (2), but were not a feature of this series.

There are a few additional signs and symptoms which should be mentioned. The presence of a "bruit" as in Case 16 is a classical sign but one apparently very rare. Beadles (5) emphasized this rarity. It is more common in arteriovenous aneurysms. It naturally would not be found in the small congenital aneurysms. Disappearance of the trigeminal pain on pressure of the carotid artery, so striking in Case 1, was not mentioned in any other cases in this series. It is, of course, analogous to the disappearance under the same circumstances of humming noises in the head, etc. in arterio-venous aneurysms. It may prove a helpful sign.

COURSE

The course depends on the etiology. The larger aneurysms, most of which are probably syphilitic in origin, often exist for years as in Hutchinson's case (Case 16). The congenital type,—once having given symptoms due to leakage—tend to have repeated episodes of leakage, one of which soon proves fatal.

TREATMENT

It is at first quite surprising that in the present series of cases, only two cases besides Case 1 have been operated upon. In Case 5 the patient was well five years after Sir Victor Horseley ligated the common carotid artery. In Case 18 relief was obtained from a similar operation. Both of these patients had relatively large aneurysms which gave symptoms before leakage. Case 1 must be one of the first in which operation has been attempted on an undoubted congenital type. Now that Symonds has pointed out the diagnosis of these cases, perhaps more operations will be attempted. I believe death in Case 1 was due to an unfortunate complicating circumstance (*vide supra*). It would seem that the situation is sufficiently analogous to that of arterio-venous aneurysms in the cavernous sinus to lead one to hope that what has been successful there will prove successful in at least part of this group. Locke (36) made a complete summary of all the cases of arterio-venous aneurysm up to 1924. There were 234 cases in which the common carotid had been ligated,

of which 154 were cured or improved. There were 34 cases in which the internal carotid artery was ligated, of which 33 were cured or improved. But only those aneurysms of this series which occurred on the internal carotid artery proximal to the Circle of Willis are analogous to arterio-venous aneurysms in the cavernous sinus. Certainly in this selected subgroup (Cases 3, 4, 5, 6, 7, 9, 14, 16, 17, 18, 20, 21, 26, 27, 31) one would expect benefit from ligation in the neck. When the aneurysms occur distal to this, it seems unlikely that much could be accomplished by such a procedure, because of the ready anastomoses. Most of the congenital cases, and certainly Case 1, would probably fall into the unfavorable group. Possibly a few, especially those on the posterior communicating artery, could be handled by ligations within the cranium. It is to be hoped that, as the diagnosis becomes more exact, some surgical technique can be developed to save this unfortunate group of patients.

SUMMARY

1. The symptoms in two patients, on whom the diagnosis of ruptured intracranial aneurysm near the junction of the internal carotid artery and the Circle of Willis was made, are reported with the autopsy findings in one case.

2. Thirty cases of aneurysm in this region which gave localizing symptoms before death are abstracted from the literature.

3. The entire series of thirty-two cases fall into five etiological groups,—mycotic, traumatic, syphilitic, arteriosclerotic, and congenital.

4. The symptomatology can be divided into two main subgroups, (a) neighborhood symptoms due to involvement of structures in this region, and (b) symptoms arising from leakage of blood into the subarachnoid space.

5. The neighborhood symptoms, except in the larger aneurysms, as a rule become manifest only after partial rupture of the aneurysm and the formation of a false aneurysm.

6. The commonest neighborhood symptoms are internal and external paralysis of the third nerve and involvement of the first branch of the fifth nerve. The third nerve was involved in every case in the series.

7. Relief of pain by obliteration of the common carotid artery in the neck was a helpful diagnostic sign in one of my cases.

8. The internal carotid artery was ligated in the neck without success in one of the newly reported cases. The possibility of relieving this condition by surgery is discussed but no conclusions are reached.

The author is much indebted to Dr. Walter Dandy, Dr. Warfield T. Longcope, Dr. James H. Means, Dr. W. G. MacCallum, and Dr. Margaret Smith for their valuable assistance.

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A COMPARISON OF THE AMYLASE CONCENTRATION IN THE SALIVA OF INFANTS AND ADULTS[1]

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This study confirms the results obtained by Nicory (1) and by Cocchi (2) that infants, both normal and premature, can digest starch from birth and that the amylase concentration in saliva increases with the age of the individual. However, the amylase concentration in the saliva of adults varies widely. Plugs of absorbent cotton were placed in the mouths of six infants and of three adults and the amount of saliva collected was determined by weight. The amylase concentration was measured viscometrically (3): 0.3 of the specimen of saliva diluted with 1 cc. of normal salt solution was added to 10 cc. of a 3 per cent starch solution at pH 7.0 and kept at 34°C. in

TABLE I

Amylase concentration in the saliva of infants and adults

SUBJECT	AGE	AMOUNT OF SALIVA COLLECTED	UNITS PER GRAM OF SALIVA
		mgm.	
Infant No. 1 (premature)	3 days	85	23
Infant No. 2 (premature)	3 days	37	28
Infant No. 3 (full term)	1 day	84	37
Infant No. 4 (full term)	3 days	53	60
Infant No. 5 (full term)	7 months	135	444
Infant No. 6 (full term)	18 months (pellagra)	167	296
Adult No. 1	24 years	123	200
Adult No. 1	24 years	60	366
Adult No. 2	29 years	93	2850
Adult No. 3	36 years	205	965

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Ostwald viscosimeters. The viscosity was determined at intervals of 3 to 10 minutes and the time required for a 20 per cent reduction in the initial viscosity was noted. The results in Table I are expressed in units of amylase per gram of saliva, *i.e.*, the amount of amylase required to reduce the initial viscosity 20 per cent in 60 minutes.

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A RADIOPAQUE BISMUTH SUSPENSION FOR ANATOMICAL, HISTOLOGICAL AND PATHOLOGICAL RESEARCH[1]

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INTRODUCTION

A radiopaque injection method which will permit studies of the vascular and lymphatic systems without endangering life may sometime be discovered. But there are serious factors requiring most careful consideration before this can be accomplished. To delineate clearly the blood vessels in various tissues requires the introduction into the circulation of some opaque or radioactive, non-poisonous element or compound.

Roentgen's prediction that the opacity of any substance to these rays was in direct ratio to its density or atomic weight was confirmed at an early period and has been strikingly illustrated recently in the evolution of cholecystography (1). Combinations of phenolphthalein and the halogens became increasingly reliable in clinical diagnosis, as the chlorine radical of lower atomic weight was replaced by that of bromine and finally by that iodine. All halogens have similar characteristics and are electro-negative so that differences in penetrability by these rays must be due to their atomic weights: Cl, 35.46; Br 79.92; I, 126.92.

Gough (2), in 1920, published the results of his own work on radiopaque injections and concisely reviewed the technique and methods of previous investigators. With a refreshing frankness, he concluded that, although some injection methods might be good, none was dependable. Furthermore, and against this I believe there will be no protest, he stated that any method should be so simple that the average skilled technician could obtain continuously reliable results. His conclusions are consoling to those who have carefully followed the tech-

[1] Received for publication December 20, 1928.

nique of many supposedly simple injection methods and have obtained results far different from those anticipated. However, where roentgenological technique, blood pressure, tissue injury, complete filling of the largest as well as of the smallest vessels, are only the more important factors essential to satisfactory injections, there is a limit to simplification. Judgment will always be required when dealing with variables, such as the differences in unit vascular structure, blood and injection pressure during or after death, caused by the contraction or relaxation of the tissues of the body.

Briefly, we find that a search for the ideal opaque element or compound began with the use of calcium (at. wt. 40.07), as reported more or less independently by Dutto, Hildebrand and Rowland in 1896. Hatschek and Lindenthal, in 1896–97, demonstrated a human hand, the vessels of which were filled with a mixture of calcium and cinnabar. This appears to mark the earliest appreciation of the necessity for greater opacity in outlining circulatory vessels. In 1899, Glew and Ind-Musgrove of England and Opitz of Germany presented beautiful specimens injected with metallic mercury, and conclusively proved Roentgen's theory concerning atomic weight and penetrability.

Then followed experiments with practically every available soluble or insoluble mineral or metal combined with water, oil, lard, wax, turpentine, celloidin and gelatin to form solutions, suspensions, pastes and emulsions. The ever-increasing realization of the possibilities of solving heretofore difficult problems through radiopaque injections has resulted in late years in a rapidly increasing bibliography. So far as this report is concerned, it seems doubtful if an extensive review of this work would compensate for the space required. These recent publications cover a surprisingly varied field of research but are readily accessible.

The recent and extended use of iodine and iodides is of value in clinical diagnosis and in limited fields of research, but is of only academic interest at present in studies of the circulation. Forty-percent sodium iodide in an aqueous solution, or sodium iodide combined with bromides, has been used intravenously in living subjects. But even with the aid of a tourniquet, diffusion into the tissues occurs so rapidly that only a fleeting opportunity is allowed for a fluoroscopic study of the localized blood supply of the arm, hand, foot or leg.

PERSONAL EXPERIMENTS

An outline of the technical problems presented during this investigation may be of value in similar studies. Each factor essential to obtain serially reliable, radiopaque injections will be more fully considered under its own title. Over seven hundred tests have been made by myself and others.

At first, all that appeared needful in this investigation was a modicum of patience in examining by x-ray those minerals, metals and their salts that were not too expensive for general use. Pure silica glass test-tubes of the same calibre and similar x-ray penetration proved efficient in quickly determining the relative radiopacities of the various substances studied. Repeated injections into animals, cadavers and fetuses were required in making final decisions concerning precipitation in the vessels, injuries to and infiltration into the tissues, pressure requirements, time limits and similar problems. To avoid roentgenological errors in technique such as might be occasioned by differences in the time of exposure, incidence of rays, focal distance and unequal periods of film development, specimens injected for comparison were x-rayed on the same plate or film. The radiopaque substances which were investigated included colloidal and non-colloidal compounds of lead, copper, silver, thorium, bromine, iodine, iron, zinc, sodium, potassium, bismuth and barium. All previous methods and formulae were used, but none proved reliable except in very limited fields of study and all required considerable experience in injection technique.

In 1921 (3), I noted that metallic or mineral salts which were soluble in water were of little value in obtaining clear, definitive radiopaque injections of the arterial tree. Microscopic study and x-ray examinations indicated the presence of an oedema due to the passage through the vessel walls of the soluble opaque medium. This infiltration into the tissues deprived the blood vessels of the substance intended to differentiate them. Also, the presence of this opaque substance in the tissues, together with the consequent oedema, prevented normal penetration by x-rays.

In several instances the circulatory system had been washed as free as possible of blood. X-ray comparisons between animals injected

when the blood had not been removed from the circulation after death, and those where cleansing of the blood vessels had been attempted, were instructive. It was evident that the injection of normal saline solution into the circulation through the aorta, even with an ample outlet for the venous blood through the incised right auricle, caused oedema. When saline solution replaces the blood *post mortem*, and then in turn is forced slowly ahead of the radiopaque suspension, infiltration into the tissues occurs. This discovery afforded additional proof that no soluble radiopaque substance such as the iodides could be used. Washing out of the blood proved to be harmful and was discontinued within three months after the beginning of this investigation. Yet it has been extraordinarily difficult to overcome this ancient fetish, which demands the absence of blood from the circulation regardless of the injection method advocated. The important action of the blood-serum in diluting the suspension as it passes into the smaller vessels permits the use in the present method of only one suspension instead of two. In the earlier experiments an injection containing low percentages of bismuth and acacia had to be followed by a suspension of much higher percentages in order to fill the smallest vessels and then the larger ones.

Further search had to be confined to some insoluble salt of high atomic weight which could be suspended or emulsified. Space and the lack of importance, so far as the final results are concerned, do not warrant an extended discussion of all of these. It might be mentioned that certain salts of lead and mercury, especially mercuric sulphide, settle out so quickly after suspension that only a very rapid injection under considerable pressure will carry any appreciable amount of these radiopaque substances into the finer vessels. The high pressure required is apt to cause distortion and rupture of the arteries, while too rapid sedimentation results in an oval rather than a circular appearance of the vessels when viewed stereoscopically. For example, injections of insoluble lead chromate obscured entirely the arterial tree of the kidney when x-rayed, and microscopic examination of sections showed serious injury to the endothelium of the vessels, thereby allowing direct passage of the opaque medium into the tissues. Once again the search for a satisfactory substance was restricted. Nothing that caused tissue injury could be used.

Experiments were finally limited to an investigation of the qualifications of an imported bismuth oxychloride. It was found that bismuth oxychloride was the most suitable radiopaque substance; and attention was at once given to discovering a satisfactory medium in which this could be suspended. In this search there were certain definite limitations. Any substance used for a suspension must have no dehydrating effect on the tissues, must not diffuse through the vessel walls and must cause no injury to the endothelium of the vascular or lymphatic systems. The suspending element or compound should be readily soluble in water and usable at any temperature. It should have a cohesive action and yet pass through a 23-gauge needle without clogging. Acacia, pulverized, met all of these requirements. In the earliest experiments acacia was used primarily as an aid in suspending the mass because the smallest particles of the imported bismuth never measured less than 8.5 microns. But when, in 1922, a more finely divided form of bismuth oxychloride was discovered, the cohesive action of acacia became of paramount interest. This specially prepared American bismuth is so finely divided that it passes through the capillaries into the veins. Only through the cohesive action of acacia could the particles be held together and prevented from entering the venous system (Fig. 1). By changing the percentages of the acacia and bismuth, the opaque particles can be formed into groups of a predetermined size. The method, two years before publication, was given to Reichert (4, 5, 6) for use in serial studies of normal tissues, and later to Graham (7) for serial arterial injections of pathological material. To demonstrate its dependability in other hands, illustrations from the publications of these investigators are included (Figs. 2 to 4).

FIG. 1. AN ARTERIAL INJECTION WITH THE BISMUTH RADIOPAQUE SUSPENSION OF THE ARM AND HAND OF AN EIGHT MONTHS' FETUS

The injection was made through a No. 22 G. hypodermic needle passed into the left ventricle and aorta. The entire body showed a similarly clear definition of the arterial circulation. Roentgenograms of several of these injected fetuses and new-born babies were demonstrated at the annual meeting of the American Association of Anatomists in 1921. The presence of only one palmar arch is interesting, but not a rare occurrence at any age. (Hill: *Johns Hopkins Hosp. Bull.*, July, 1924, Vol. 35.)

FIG. 1

UNIV. OF MICH.

Bismuth oxychloride. The bismuth oxychloride imported in 1917 was ideal for certain types of roentgenological investigations of the collateral circulation. The smallest indivisible particles never measured less than 8.5 microns, and the radiopaque suspension caused no confusion by passing into the venous system.

FIG. 2. ARTERIAL INJECTION WITH BISMUTH SUSPENSION OF A DOG 12 DAYS AFTER DIVISION OF THE ABDOMINAL AORTA

(Reichert: *Johns Hopkins Hosp. Bull.*, December, 1924, Vol. 35)

But even before the depletion of this supply of bismuth, a substitute was being sought. The imported compound, to a moderate but microscopically noticeable degree, irritated delicate tissues when applied in powdered form or when used in suspensions containing a high percentage of bismuth. Several manufacturing chemists and pharmaceutical firms very courteously sent samples of their products and attempted to produce, through re-milling and by fresh precipitations, a bismuth oxychloride with the desired qualifications. Finally,

in 1922, a finely divided, non-irritating, non-poisonous brand of this metallic salt was discovered under the trade term of "Cosmetic Bismuth." It was manufactured by the Powers-Weightman-Rosengarten Company; Merck and Company are now their successors. The Mallinckrodt Chemical Works also manufacture an equally suitable product.

These relatively uniformly and finely divided preparations of bismuth are extremely advantageous because the smaller the particulate

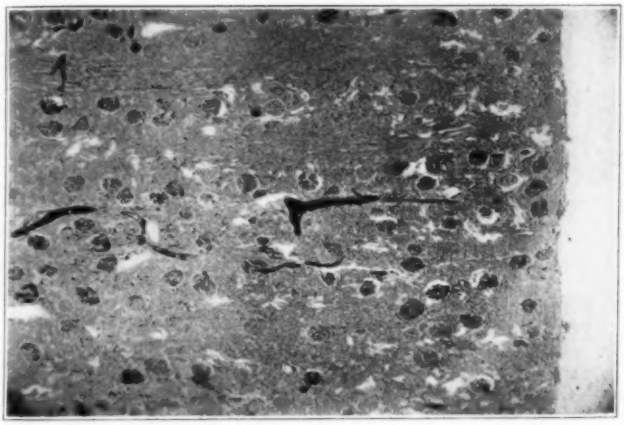

FIG. 3. PHOTOMICROGRAPH (VERY LOW POWER) OF INJECTED RENAL CORTEX SHOWING INJECTION MASS IN INTERLOBULAR ARTERIES, IN GLOMERULAR ARTERIES AND IN GLOMERULI AS DENSE BLACK MATERIAL

(Graham: *Am. Jour. Pathology*, January, 1928, Vol. 4, No. 1)

matter, the longer it will remain in suspension. Also, the more finely divided the radiopaque substance when in suspension, the more compact will be the filling of both the large and the small blood vessels because of the absence of interspaces between the particles.

Acacia. As noted, any vehicle for suspending radiopaque substances should be readily soluble in water, should remain in solution at ordinary temperatures and should cause no tissue injury. Also, if the suspension is to be available for immediate use, it should require no special preparation. If an injection mass has to be heated in order

to flow easily through blood vessels or lymphatics, then the part to be injected must likewise be thoroughly warmed to a similar temperature.

FIG. 4. ROENTGENOGRAM OF NORMAL ARTERIAL TREE. KIDNEY FROM A MAN, 40 YEARS OF AGE, DYING OF CARCINOMA OF THE LIVER
(Graham: *Am. Jour. Pathology*, January, 1928, Vol. 4, No. 1)

This complicates any method where immediate injection is desired. Were bismuth oxychloride not so finely divided, acacia, except in high percentages, would not be satisfactory. Red oxide of lead, for

example, requires a suspension in a fluid of relatively high specific gravity.

Acacia causes no injury to tissues, remains in solution indefinitely, prevents the passage of the suspension through the capillary wall and has a most important cohesive action. This action is one of the factors upon which this injection method depends.

By varying the amounts of the acacia used, the bismuth particles can be loosely or firmly bound together into microscopic groupings of any desired size. To penetrate the capillary bed and at the same time fill the circulatory system, a suspension of 20-per-cent bismuth oxychloride in an aqueous solution of 11-per-cent acacia is usually satisfactory. These percentages had to be changed from 17-per-cent bismuth and 10-per-cent acacia when the American bismuth replaced that of foreign manufacture (3). The groups of radiopaque particles in a suspension of this strength, when compared microscopically with human red blood cells, vary in size from 8 to 50 microns. The larger groups might be expected to block the passage of the suspension into the smaller arterioles and capillaries. That this does not occur is clearly proved by histological examination. The percentages of bismuth and acacia mentioned produce only loosely bound particulate matter. By increasing the bismuth content to 40-per-cent and by using a solution of 25-per-cent acacia, these groups are so large and so closely knit that only the larger vessels can be penetrated.

That acacia dissolves readily in water and does not change in consistence at room temperatures; that it has negligible radiopacity and that it possesses a remarkable cohesive action are important. In appreciable amounts, it prevents collapse of large, thin-walled vessels such as the vena cava. In the percentages ordinarily used, it aids directly in preventing leakage from blood vessels during dissection.

Semi-filtration. Semi-filtration is the term which I have applied to a method by which loosely combined masses of bismuth and acacia measuring from 3.5 to 250 microns are aggregated into relatively uniform groups of predetermined size.

Pulverized acacia readily dissolves in water, but the amorphous, finely-divided, insoluble bismuth oxychloride, even as a dry powder, has a tendency to form macroscopic clumps. Consequently, when

the bismuth is suspended in a solution of acacia, clumps are present. Such a mixture is of comparatively small value except in gross radiopaque injections. Particles of bismuth, uncombined with acacia and measuring from 0.5 to 4.5 microns, may be present in such a suspension together with closely grouped particles which are larger than the lumen of the small vessels.

By pouring the originally mixed bismuth and acacia solution through cloth, three effects are obtained: separate particles of bismuth are forced into a cohesive combination through the action of the acacia, large loosely bound groups are divided, and any firmly knit clumps are withheld from passing into the final suspension. Thus, depending upon the mesh of the cloth and upon the percentages of the bismuth and acacia used, the suspension will be composed of practically uniform groups of any desired size.

Until 1924, dependence was placed upon the number of layers of cloth through which the suspension was passed. The more layers of cloth, the smaller were the particulate groups. A suspension of the foreign bismuth frequently required several semi-filtrations. At times a pestle was necessary in order to produce an injection mass that would penetrate to the capillary bed. Percentages lost their meaning when varying quantities of bismuth remained on the filtering material. The bismuth now used is composed of dry particles which are only two-thirds of the size of those found in the imported brand, and measure 0.5 to 4.5 microns. With the adoption of the American bismuth it was possible to simplify the older and more difficult method of semi-filtration. The former technique, which was evolved in order to obtain the smallest particulate groups, was changed to one which would produce groups sufficiently large to resist passing into the capillaries. The dependence upon layers of fabric required studies of the final suspension. The mixture had to be examined microscopically and tested with hypodermic needles of different gauges.

In 1923, an investigation of various textiles resulted in a simplification and a greater degree of standardization in preparing this radiopaque injection. Dependence is now placed upon the mesh and only one layer of fabric is required. The closeness of the weave determines the sizes of the particles or particulate groups that will appear in the suspension. The more strands per square inch in the material, the

smaller will be the meshes through which the radiopaque substance must pass and the smaller will be the particulate groups. Conversely, the coarser the cloth, the larger will be the groups passing through. In selecting the material, bolting cloth, silk, linen, mixtures of linen and cotton, loosely woven cotton and wool may be considered in the order given in preparing suspensions containing very fine, fine, medium and large particles or particulate groups. The percentages of bismuth and acacia used are closely related to the mesh required, and will be considered in the next section of the report.

Preparation of the bismuth suspension. The preparation of this radiopaque bismuth suspension requires about ten minutes. The powdered acacia is dissolved in boiling water. A paste is prepared of a portion of the acacia solution and the proper amount of bismuth oxychloride. This paste is then added slowly to the bulk of the acacia solution and boiling water is added to the mixture to obtain the necessary percentages. The suspension as prepared for general use is poured through "tea towelling" composed of about 40-per-cent linen and 60-per-cent cotton. For this general formula the warp should contain about 59 threads per linear inch and the woof 43. The towelling must have been thoroughly cleansed of "sizing" by boiling in soap and water and then washed in warm water. The bismuth suspension, if freshly prepared, remains warm. The towelling should be rinsed in warm water before being used.

The wet towelling, or other textile chosen, should be laid over the rim of a funnel with a cup-shaped base so that it does not come in direct contact with the sides of the funnel. This permits a more rapid passage of the suspension through the cloth. Forced straining vitiates the usefulness of the semi-filtration. If the suspension has been prepared and kept for several days or weeks, it should be shaken, stirred, warmed and again poured through the towelling.

Once prepared, the suspension may be used immediately, if not too hot, or at intervals during a period of several weeks. Bismuth apparently has a moderate degree of germicidal action which prevents bacterial growth and the spread of fungi. Boiling, however, does not affect the physical properties of the suspension and is recommended as the simplest and most convenient method when sterilization is desired or when the suspension is to be kept for several months.

Judgment is essential in deciding what percentages of bismuth and acacia will best meet the requirements of different types of investigation. At first, the details necessary for each separate problem were given, but it soon became evident that such a procedure lessened the value of the method. It is impossible to tabulate data concerning the injection of blood vessels, lymphatics, sinuses, cerebral ventricles and tubular structures, such as the ureters, as well as organs composed of markedly different vascular units. Also, the differences in various species of animals require consideration. Fortunately, however, when once the factors governing this method are understood, the formula given for general use can be quickly adapted to meet the special requirements of new problems.

As will be readily understood, higher percentages of bismuth and acacia require more loosely woven textiles for semifiltration, produce proportionately larger groups of the particulate matter and more firmly combine the bismuth particles. Conversely, low percentages of bismuth and acacia when passed through finely woven material, such as silk, produce a suspension containing smaller and more loosely grouped particles which will penetrate the lumen of the smallest vessel.

To prepare 500 cc. of this radiopaque suspension according to the formula for general use, about 250 cc. of distilled water are brought to a boil in a 1000 cc. beaker. The general formula requires an 11-per-cent solution of acacia in which is suspended 20-per-cent bismuth oxychloride. Consequently, 55 grams of pulverized acacia are slowly dissolved in the 250 cc. of water. Boiling is no longer essential when the solution is completed. The 1000 cc. container is then tilted to an angle of 45 degrees and 100 grams (20 per cent) of the Merck or Mallinckrodt bismuth oxychloride are carefully rubbed into a paste by using a spatula against the side of the beaker. As the paste composed of the acacia solution and the bismuth is formed, it is allowed to enter the solution until all of the bismuth is in suspension. Sufficient water to complete the required 500 cc. is then added to the mixture. While still warm, the suspension is poured through the towelling in the manner already described.

The maximal and minimal percentages of bismuth, which so far have met all requirements, range from 5 to 40 per cent, while the solu-

tion of acacia varies between 2 and 25 per cent. When the highest percentages of each are used, the resultant mixture becomes a paste and requires a very loosely-woven textile for semi-filtration. Whereas, if the suspension contains only the lowest percentages of these substances and has been passed through a fine mesh fabric, such as silk or linen, a few of the bismuth particles may appear separately and the loosely bound groups will be small enough to penetrate the minute lumen of lymphatics or the smallest channels.

Injection technique. The technique of injecting the radiopaque suspension differs only slightly from the methods generally used in filling arterial, lymphatic and other vessels. More attention should be devoted, however, to maintaining the steady digital injection pressure, to free drainage of the venous system in order to avoid back pressure, and to the observable signs indicating the penetration of the suspension.

Syringes of the Luer type containing 1, 2, 5, 10 or 20 cc. are recommended. The glass construction allows the investigator to watch for air bubbles, to observe the rapidity of flow and to prepare for refilling the syringe. Metal syringes of 50 or 100 cc. capacity are also advisable for extensive injections. These syringes are usually so constructed that by means of a nozzle they can be attached by a short piece of rubber tubing to a glass cannula which has been introduced into an artery or vein. For still more extensive injections the current methods of injection by gravity or pressure pump are used. Because of the adhesive action of the acacia, it is advisable to wipe the piston of the syringe with oil before and during injections.

Whether the animal is anesthetized and killed during the injection, or whether it is killed just before injection makes no difference in the final results. But if the suspension is injected directly into the heart or into the venous system the animal dies almost instantaneously from the formation of emboli.

After considering the "time limits" when injection is possible, the condition and preservation of the tissues, and the proper consistence of the suspension, perfect arterial filling of the circulatory system of new-born babies, and of dogs, cats or other animals of a similar size may be confidently expected. When a complete filling of the arterial circulation is desired, the injection is made through the aorta. Back pressure is relieved by incising the right auricle and ventricle.

After a few trial experiments, it will be found that an arterial injection of the whole body can be completed in less than thirty minutes. From the beginning of anesthetization until the animal had been x-rayed, the average time has been about 25 minutes when the work was done by students. Perfect injections of the vascular system of new-born babies require not more than 15 minutes. The actual time necessary for slowly injecting an organ averages 8 minutes.

Separate organs may be injected radioscopically whether *in situ* or after removal from the body. In either case the afferent and efferent blood vessels must be ligated as soon as possible.

Except in rare instances, when autopsy material is being used, there are no torn vessels nor injured surfaces. But should such injuries be present or occur, the ruptured vessel must be ligated and the bleeding area cauterized.

Pressure and indications of complete injection. Manometric control of the pressure required during injections is valueless as a guide in completely filling the vascular channels. Complete injections of the circulatory system depend upon certain observable signs. The gradual penetration of the intensely white bismuth into the anterior ciliary arteries and their radiating branches indicates the progress of the suspension through the cerebral vessels. Incisions through the epidermis of distal parts demonstrate the passage of the bismuth into the capillaries. A grayish coloring or a mottling which gradually becomes homogeneous is an index of the complete injection of an organ such as the liver or the kidney. Under no circumstances, as explained above, should attempts be made to wash out the blood from the vascular bed with saline solution before injecting the radiopaque suspension. Failure to observe this rule, results in uniformly poor specimens.

X-ray technique. Radiographing injected post-mortem specimens permits the use of a technique which would be dangerous in clinical work. When there is no occasion to guard against injury to living tissues, the time element as well as the character of the rays require no consideration. Consequently, there is no limit to the length of the exposure, character of the rays and the number of plates taken. Certain factors can be standardized, such as the focal distance, usually one meter or more, the milliamperage and the kilovoltage. There will be no need, of course, to resort to screens. Since 1920, I have found

that the most satisfactory results have been obtained with medium soft rays. A standard of 10 to 15 ma., with a 3-inch gap and the use of 25 kilovolts delineates the vessels and differentiates tissues of various densities. Thus the only variable factor is the time element which depends entirely upon the penetration required.

Stereograms and fluoroscopic studies should be made immediately after the injection is completed. No effusion into the tissues is then present, and the best results are obtained at this time or after a period of 24 hours. Within six to eight hours after an injection, a slight and transient infiltration of the tissues by the water used in the suspension may occur and radiograms will be less clear. Specimens may be preserved by refrigeration or placed in fixing fluids for an indefinite period. Under no circumstances should formalin be used as a preservative if circulatory investigation of the bones is contemplated. The slow decalcifying action of formalin destroys the lines of ossification. This was especially noted in radiographing valuable embryonic specimens.

Time limits for injection. Before rigor mortis occurs, tissue changes are so slight that injection is easily accomplished. But there appear to be three distinct periods after death; the time before, during and after rigor mortis. These periods vary greatly. This variance depends upon the previous health and size of the individual animal; the temperature at which the specimen has been kept after death and before refrigeration; and chemical factors not entirely understood. During the second stage, that of rigor mortis, a complete injection is usually not possible.

After rigor mortis, there occurs a third period when once again complete injections are dependable. This was verified by Reichert and several colleagues who used this method both before and after its preliminary publication in 1924. It is disconcerting that these three periods cannot be definitely timed. A decision as to injection before rigor mortis is not difficult, but the interim before the third period can be determined only experimentally. The method by which I have been able to decide approximately as to this time is by cutting certain vessels, such as the radial artery or the saphenous vein. When following a very moderate massage, a watery, sanguineous fluid flows from such an incised vessel, perfect injections are obtained.

Babies in rigor mortis have been placed in the refrigerating rooms, then later thoroughly warmed by immersion in saline solution and tested in this manner. They were then either injected, or again refrigerated until the proper time for injection.

In dealing with separate organs, such as the heart, spleen, pancreas, kidneys, liver, sexual glands or amputated parts, all of the larger blood vessels, both arteries and veins, should be ligated before removal from the body. The organs should be immediately injected or else be refrigerated and protected from drying. Graham achieved his complete series of renal injections in this manner although in one instance a kidney had been preserved for eight days (Figs. 3 and 4). I have found that during the third period the circulation is equally well shown even at the end of several weeks or months. When the injection of an organ is to be made, the veins should be opened and all of the larger arteries injected. There must be no back pressure. Clamps should be applied to any small vessels where leakage is noted by the appearance of the white bismuth suspension. When the operation is completed the vessels must again be ligated, the organ should be carefully washed and then thoroughly dried with gauze before x-ray records are made. If there be any doubt as to the penetration of the suspension into all areas, a roentgenogram can be taken or the part may be examined fluoroscopically. This is seldom necessary.

Coloring, sectioning and clearing bismuth preparation. Frequently, questions are asked concerning the advisability of adding some coloring matter to the bismuth suspension. So far there has been no apparent need for such coloring because attempts at radioscopic arterial as well as venous injections in the same specimen lead to confusion. Only stereoscopically is it possible to differentiate the small vessels in radiograms of a single injection. The intense white of bismuth is as clearly outlined macroscopically in cleared preparations as is India ink.

Bismuth oxychloride is affected by no ordinary acids, alkalies or oils and in suspension does not flow readily from the larger vessels of sectioned areas. In small vessels the acacia holds the bismuth firmly. Any of the usual clearing methods can be used and the white bismuth clearly delineates the vessels.

Bismuth oxychloride in suspensions up to 40 per cent does not injure

the most delicate membranes. Blocks of tissue may be prepared and sectioned by any of the customary methods. The usual laboratory stains change the white bismuth into a non-granular black as may be noted in the illustrations of the injected glomeruli (Fig. 3). This was noticed in 1922 after injections and microscopic studies had been made of practically all organs.

SUMMARY

A method using bismuth oxychloride (Merck's "Cosmetic Bismuth" or Mallinckrodt's "finely divided bismuth oxychloride") suspended in a solution of gum acacia has been found to be most satisfactory for post-mortem radiographic study of the vascular systems. For most purposes a suspension of 20-per-cent bismuth oxychloride in 11-per-cent solution of acacia gives excellent delineation, but for specific tissues the percentages of both the bismuth and the acacia must be varied to secure optimal results. The acacia serves as an agent to aggregate the finely divided particles of bismuth, and by employing cloth filters of various meshes unit-masses of any desired size may be obtained. Tissue injected with this radiopaque suspension may be studied microscopically either as cleared specimens or in stained histological sections; in both, the bismuth is clearly delimited from the surrounding tissues.

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BOOK REVIEWS

The Glands Regulating Personality. By LOUIS BERMAN, M.D., Associate in Biological Chemistry, Columbia University. Second revised edition. 341 pp. $3.50. (*MacMillan and Company, 1928*).

The author of this book is a biochemist who holds strongly to the belief that the shape and action of the human body and mind depend on the endocrine secretions. As man is as old as his arteries so an individual is what he is because of his gland formula. Beginning with a few chapters describing the physiology of each of the endocrine glands he follows with the effects produced by a marked pathological derangement of one or more of them and the changes from infancy to senility as influenced by them. He devotes several chapters to kinds of personality showing how they may be altered, partly through environment but largely through an alteration of the endocrine balance. These statements are exemplified by a description of several well-known notables,—Napoleon, Oscar Wilde, Florence Nightingale, and others—with a discussion as to why they may be considered gland types. He ends with a prophecy that, as the exact chemical nature of each hormone is determined, a powerful method of controlling human activity will be found, which will aid the physician and the eugenist. The author has certainly given a readable presentation of a very intricate subject written in a non-technical style which will appeal to the intelligentsia among the laity though it contains very little not already known to the physician.

F. R. S., JR.

Schizophrenia (Dementia Praecox). Association for Research in Nervous and Mental Disease. A Series of Research Publications. Volume V. 491 pp. $7.50. (*Paul B. Hoeber, New York, 1928*).

The book presents a picture of the present formulation of the whole schizophrenia question and of the investigations which are undertaken in the different hospitals of the country. The first chapter is devoted to an historical survey which Adolf Meyer presents on a broad basis so that it is really the history of modern psychiatry as a whole. It is interesting to note how far-reaching is the influence of the three outstanding modern investigators (Kraepelin. Bleuler and Adolf Meyer). The contributions in this book show clearly that, while Kraepelin's rigid nosological concept still influences greatly continental psychiatry, American psychiatry works entirely under Bleuler's (psychodynamic and psychoanalytic) and Meyer's (special personality reacting to life situations) guidance. Brill formulates Bleuler's most recent viewpoint, inclined to a rather rigid acceptance of a constitutional and somatic basis, while Campbell discusses the symptoms in a broad way based on Meyer's concept of reaction types. Some authors point to the importance of

having an elastic concept in which admixtures can be accepted and psychogenic as well as somatic factors (Sullivan Hutchings, Gregory, Menninger, Jelliffe). Other presentations are devoted to solve the problem with post-mortem (Dunlap, Freeman, Lewin, Fulston); endocrinological and biochemical (Bowman, Whitehorn); roentgenological (Henry); and psychogalvanic (Syz), investigations. Heredity and constitution receive an interesting discussion (Barrett, Myerson, Raphael, Amsden). The importance of statistics is illustrated (Pollack). Psychoanalytic interpretations attempt to explain schizophrenic language (White), and art productions (Lewis). Prognosis (Strecker) and treatment (Hamilton) are presented very inclusively. All the publications reveal an original spirit, taking critically into account the modern European schools, but using their ideas in a broad way.

O. D.

BOOKS RECEIVED

A text-book of Surgery. For Students and Physicians. By W. WAYNE BABCOCK, A.M., M.D., F.A.C.S. With 1041 illustrations and 9 plates in color. 1928. 8°. 1367 pages. W. B. Saunders Company, Philadelphia. $10.00.

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